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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/262,126	Miller et al.
Examiner	**Art Unit**
Manjunath N. Rao	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 26, 2001*

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-51* is/are pending in the applica

4a) Of the above, claim(s) *16-26 and 41-51* is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-15 and 27-40* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 2

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. Claims 1-51 are now pending in this application.

Election/Restriction

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-15, 27-40, drawn to modified pullulanase and its composition, classified in class 435, subclass 210.

II. Claims 16-26 and 50-51, drawn to nucleic acids, vectors and host cells, classified in class 435, subclass 320.1.

III. Claims 41-49, drawn to a process for saccharification of starch, classified in class 435, subclass 275.

3. The inventions are distinct, each from the other because of the following reasons:

4. Inventions I and II are patentably distinct from each other. The polypeptide of group I, the polynucleotide of group II, each comprise amino acid sequences and nucleotide sequences which are chemically unrelated, do not require each other for practice; have separate utilities, such as use of the group I polypeptide to catalyze a saccharification reaction versus the use of polynucleotide in a hybridization reaction and are subject to separate manufacture and sale. The groups have acquired separate status in the art and separate fields of search.

5. Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polypeptides can be used for raising specific antibodies as opposed to its use in a saccharification reaction.

6. Inventions III and II are patentably distinct from each other. The process for saccharification neither uses nor makes the product of group II, namely the nucleic acid and host cells. The groups are subject to separate manufacture and sale. The groups have acquired separate status in the art and separate fields of search.

7. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

8. During a telephone conversation with Christopher Stone on 4-12-2000 a provisional election was made with traverse to prosecute the invention of group I, claims 1-15, 27-40. Affirmation of this election must be made by applicant in replying to this Office action. Claims

16-26 and 41-51 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

9. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Priority

10. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Drawings

11. This application has been filed with drawings that have been objected to by the Draftsperson. Please see the attached form PTO948 for details.

Claim Objections

12. Claims 2, 4 are objected to because of the following informalities: Claims 2 and 4 recite the word "Gram" beginning with a small letter "g". Appropriate correction is required.

13. Claims 4, 5, 9, 10, 12, 15, 35, 36 are all objected to because of the following informalities: Claims 4, 5, 9, 10, 12, 15, 35, 36 all recite biological names in regular font. All biological names of genus and species should be recited in italics or under lined. Appropriate correction is required.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 15 recites the phrase "is essentially eliminated". It is not clear to the Examiner as to whether applicants mean that the protease activity is totally eliminated or eliminated to a lesser degree. Amending the claim to recite "is completely eliminated" or simply "eliminated" would overcome this rejection.

16. Claim 33 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 33 recites the phrase and/or. The use of the above phrase renders the claim

indefinite as it forms a improper Markush group as well as does not indicate a clear limitation of the claim.

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 1-13, 15, 27-30, 33-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a modified pullulanase enzyme with amino acid SEQ ID NO:2 or a modified pullulanase beginning at amino acid residue 99 or 103 of SEQ ID NO:2, does not reasonably provide enablement for any modified pullulanase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 1-13, 15, 27-30, 33-40 are so broad as to encompass any modified pullulanase including those with a deletion of 98, 100, 102, 200 or 300 amino acids or any recombinantly modified pullulanase enzyme from any source. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of modified pullulanase enzymes broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and to obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence,

if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the pullulanase enzyme with SEQ ID NO:2.

While enzyme isolation techniques and recombinant techniques are known, it is not routine in the art to screen multiple sources, multiple substitutions, or multiple modifications, as encompassed by the instant claims, and the reasonable expectation of success in obtaining the desired enzyme are limited due to the complexity of the huge number of microorganisms, animals and plants that need to be analyzed and the result of such isolation from an extremely large number of sources is unpredictable.

The specification does not support the broad scope of the claims which encompass all modified pullulanase because the specification does **not** establish:(A) a rational and predictable scheme for isolation and characterization of any modified pullulanase from any given source with an expectation of obtaining the desired biological activity and function; (B) the general tolerance of pullulanase enzymes to modification and extent of such tolerance; and (C) the specification provides insufficient guidance as to which of the infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any modified pullulanase enzyme of any microorganism or animal

or plant. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a modified pullulanase having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

19. Claims 1-13, 15, 27-30, 33-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-13, 15, 27-30, 33-40 are directed to polypeptides corresponding to the sequence of SEQ ID NO:2 and variants of SEQ ID NO:2. Claims 1-13, 15, 27-30, 33-40 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides derived from SEQ ID NO:2 including modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue in SEQ ID NO:2 and fragments of SEQ ID NO:2 that have not been disclosed in the specification. No description has been provided of the modified polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:2 has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides. The

specification does not contain any disclosure of the structure of all the polypeptide sequences derived from SEQ ID NO:2, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structure and function. Therefore many structurally and functionally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

20. Claim 5 is rejected because the invention appears to employ novel bacterial strain. Since the bacterial strain is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed bacterial strain is not fully disclosed, nor have been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the bacterial strain. The specification does not disclose a repeatable process to obtain the bacterial strain and it is not apparent if the DNA sequences are readily available to the public.

Accordingly, it is deemed that a deposit of bacterial strain should have been made in accordance with 37 CFR 1.801-1.809.

It is noted that applicants have deposited the organisms but there is no indication in the specification as to public availability. If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;

2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and

4. the deposit will be replaced if it should ever become inviable.

Claim Rejections - 35 USC § 102

21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

22. Claims 1, 2, 6, 13, 27-28, 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Albertson et al. (Biochim. Biophys. Acta. 1997, Vol 1354(1):35-39) or McPherson et al. (Biochem. Soc. trans., 1988, Vol 16(5), 723-724). This rejection is based upon the public availability of a printed publication. Claims 1, 2, 6, 13, 27-28, 38 of the instant application are drawn to a modified pullulanase isolated from either a Gram positive or negative bacteria, wherein the modification is a deletion of about 100 amino acids from the amino terminus (claims 1, 2, 6), a modified pullulanase produced by a host cell comprising the nucleic acid encoding the mature pullulanase (claim 13), a composition comprising the said modified pullulanase (claims 27-28, 38). Albertson et al. and McPherson et al. disclose a modified pullulanase enzyme which lacks about 127 amino acids (Albertson et al.) or 170 amino acids (McPherson et al.) from the amino terminus. The reference also discloses a modified pullulanase prepared by culturing a host cell comprising a nucleic acid encoding a mature pullulanase enzyme. Thus Albertson et al. or McPherson et al. anticipate claims 1, 2, 6, 13, 27-28, 38 of this application as written.

23. Claims 1, 2, 4, 13, 27, 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Murooka et al. (J. Biol. Chem., 1989, Vol. 264(29):17524-31) or McPherson et al. (Biochem. Soc. trans., 1988, Vol 16(5), 723-724). This rejection is based upon the public availability of a printed publication. Claims 1, 2, 4 and 27 of the instant application are drawn to a modified pullulanase isolated from either a Gram Positive or Gram negative bacteria which includes *K.pneumoniae* and *K. aerogenes* , wherein the modified pullulanase is produced by a host cell comprising the nucleic acid encoding the mature pullulanase (claim 13), a composition comprising the said modified pullulanase (claims 27-28, 38). While McPherson et al. disclose a modified pullulanase enzyme from *K.pneumoniae*, Murooka et al. disclose a modified pullulanase isolated from *K.aerogenes*. Thus Murooka et al. or McPherson et al. anticipate claims 1, 2, 4, 13, 27 and 38 of this application as written.

24. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

25. Claims 1-3, 5, 11-14, 27, 33- 39 and claims are rejected under 35 U.S.C. 102(e) as being anticipated by Deweer et al. (US 6,074,854, filed 12-23-1997, issued on 6-13-2000). This rejection is based upon the public availability of a patent publication. Claims 1-3, 5, 11-14, 27,

33- 39 of the instant application are drawn to a modified pullulanase isolated from either a Gram Positive or Gram negative bacteria which includes *B.deramificans strain T89.117D*, wherein the modified pullulanase has at least one amino acid such as alanine added to the amino terminus (claims 11-12), is produced by a host cell comprising the nucleic acid that has 70% identity to SEQ ID NO:1, encoding the mature pullulanase (claim 13-14), a composition comprising the said modified pullulanase (claims 27) further comprising another enzyme such as a glucoamylase isolated from any *Aspergillus* strains such as *A.niger, A.awamori* and *A.foetidus* (claims 33-36), a composition which is in solid form or liquid form or comprising 60% modified pullulanase (claims 37-39). Deweer et al. disclose an identical pullulanase from B.deramificans (see the entire document, especially claims 1-21). Thus Deweer et al. anticipate claims 1-3, 5, 11-14, 27, 33- 39 of this application as written.

Claim Rejections - 35 USC § 103

26. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

27. Claims 1-15 and 27-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deweer et al. (US 6,074,854, filed 12-23-1997, issued on 6-13-2000), Murooka et al. (J. Biol. Chem., 1989, Vol. 264(29):17524-31) or McPherson et al. (Biochem. Soc. trans., 1988, Vol

16(5), 723-724) and Albertson et al. (Biochim. Biophys. Acta. 1997, Vol 1354(1):35-39). This rejection is based on printed publications and a patent. Claims 1-15 and 27-40 in this instant application are drawn to a modified pullulanase from a gram positive or Gram negative bacteria such as B.deramificans T89.117D or K.pneumoniae or K.aerogenes, wherein the modification is a deletion of 98, 100, 102, 200 or 300 amino acids from the amino terminus or the addition of at least one amino acid such as alanine to the amino terminus, wherein the modified pullulanase is produced by culturing a host cell comprising a nucleic acid which is at least 70% identical to SEQ ID NO:1 encoding a pullulanase which starts at amino acid residue 99 or 103 and wherein the host cell is *B.licheniformis* in which certain proteases are inactivated or eliminated. The claims are also drawn to compositions comprising the above modified pullulanase and compositions further comprising additional enzymes such as glucoamylase isolated from Aspergillus strains and wherein the modified pullulanase is 60 or 80% of the composition and wherein the composition is in the solid or liquid form.

Deweer et al. teach a modified pullulanase obtained from a Gram positive bacteria such as *B.deramificans* T89.117D produced by a method of culturing a host cell such as *B.licheniformis* in which certain protease genes have been inactivated. The reference also teaches the modification comprising the addition of at least an amino acid such as alanine to its N-terminus and the host cell comprising a nucleic acid which is more than 70% identical the SEQ ID NO:1 (see sequence alignment). The reference teaches the compositions either in the solid form or liquid form comprising pullulanase wherein it is of the order of 60% of the total

enzyme concentration. The reference also teaches compositions comprising additional enzymes such as glucoamylase isolated from Aspergillus strains (see claims in the reference). However, the reference does not teach modification of pullulanase by way of deletion of N-terminal amino acids or pullulanase which being from residue 99 or 103 or wherein 98, 100, 102, 200 or 300 amino acid residues from the N-terminal have been deleted. The reference also does not teach pullulanase isolated from *Klebsiella* strains.

Murooka et al. or McPherson et al. teach modified pullulanase isolated from *Klebsiella aerogenes* and *K. pneumonia*. the reference teaches the modifications in the form of deletion of amino acids from the N-terminal end. McPherson et al. teach the modification of deleting nearly 170 amino acid residues from the amino terminal end which leads to approximately 30% higher activity than that of the native enzyme. Murooka et al. also teach the deletion of a pentapeptide at the amino terminal end of a native *K.aerogenes* pullulanase to make a modified pullulanase.

Albertson et al. also teach the modification of a pullulanase wherein nearly 381 nucleotides from the 5' region of the cDNA encoding a pullulanase was deleted resulting in a N-terminal truncated pullulanase. It appears that experiments involving truncation of N-terminal by way of deleting amino acid residues at the N-terminus was well known in the art. These experiments appears to have been performed to determine the nature and the location of secretion signal, catalytic site, transport across membrane and secretion into liquid medium.

It would have been obvious to one skilled in the art at the time the invention was made to combine the teachings of Deweer et al. with that of Murooka et al. or McPherson et al. and

Albertson et al. to make a modified pullulanase in which N-terminal amino acids have been deleted or few amino acids are added to the N-terminal end. Murooka et al. or McPherson et al. teach that one would be motivated to do this in order to locate the secretion signal or the catalytic site in the pullulanase. It would also be obvious for one skilled in the art to eliminate or inactivate the protease genes such as Carlsberg protease or endo Glu C protease as Deweer et al. teach such inactivation of proteases such that the heterologous protein is not digested by the endogenous proteases. One would have a reasonable expectation of success since Deweer et al. provide the nucleic acid encoding the pullulanase from *B.deramificans* in a host cell such as *B. licheniformis* in which protease genes have been inactivated and also provide the compositions of pullulanase and Murooka et al. or McPherson et al. or Albertson et al. teach the pullulanase from *Klebsiella sp.* and the reason for deletion of N-terminal amino acids.

Therefore the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath Rao whose telephone number is (703) 306-5681. The Examiner can normally be reached on M-F from 6:30 a.m. to 3:00 p.m. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, P.Achutamurthy, can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Manjunath N. Rao

June 1, 2001